

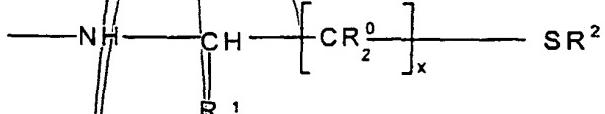
CLAIMS:

5 1. A collagenic peptide modified by grafting free or substituted thiol functions borne by mercaptoamino residues, characterized:

10 • in that these mercaptoamino residues are identical to or different than each other and are exclusively grafted onto the aspartic acids and glutamic acids of the collagenic chain via amide bonds, and

15 • in that it is soluble in aqueous medium and/or in polar solvents.

20 2. The collagenic peptide according to claim 1 characterized in that at least some of the mercaptoamino residues, grafted onto the carboxylic acids of the aspartic acids and glutamic acids, correspond to the general formula (I) below:

FORMULA (I)

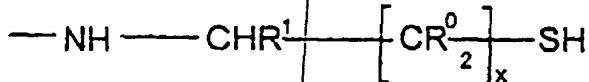
in which

- 25 • $x = 1$ or 2 ;
- $R^0 = H$ or CH_3 ;
- 30 • R^1 represents H or $COOR^3$ with R^3 corresponding to a hydrocarbon-based radical of aliphatic, aromatic or alicyclic type, preferably alkyl, alkenyl, aryl, aralkyl, alkylaryl or alkenylaryl type and even more preferably of methyl or ethyl type;

residues of formula (I) as defined in claim 2 and
in which R² corresponds to hydrogen, and
♦ in that it is crosslinkable.

- 5 5. The collagenic peptide according to claim 4,
characterized in that it comprises mercaptoamino
residues of formula (I') below:

FORMULA (I')



10 in which R¹ corresponds to H or to COOR³, with x, R¹,
R⁰ and R³ as defined above in claim 2 in the legend
of formula (I), R³ also possibly representing
hydrogen or a cation capable of forming a salt with
COO⁻, this cation preferably being Na⁺, K⁺ or Li⁺.

- 15 6. A crosslinked collagenic peptide, characterized
• in that it comprises collagenic chains linked
20 together by disulfide bridges in which the
constituent sulfur atoms belong to mercaptoamino
residues that are exclusively grafted onto the
aspartic acids and glutamic acids of the
collagenic chains via amide bonds.
• in that is obtained from the collagenic peptide as
25 claimed in claim 4 and/or 5.

- 30 7. The collagenic peptide according to any one of
claims 1 to 6, characterized in that it comprises
grafts G, which are different than mercaptoamino
residues (in particular those as defined above in
claims 1 to 6), attached to at least some of the
free amine moieties of the collagenic chain, via
amide bonds, G being an acyl comprising a

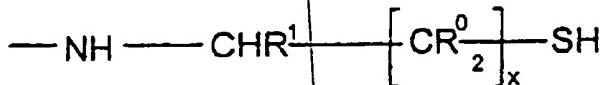
AMENDED SHEET

Newly filed

residues of formula (I) as defined in claim 2 and
in which R² corresponds to hydrogen, and
♦ in that it is crosslinkable.

- 5 5. The collagenic peptide according to claim 4,
characterized in that it comprises mercaptoamino
residues of formula (I') below:

FORMULA (I')



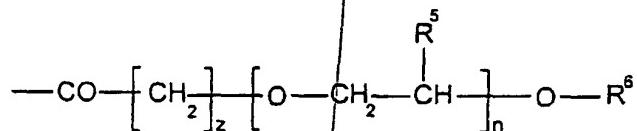
10 in which R¹ corresponds to H or to COOR³, with x, R¹,
R⁰ and R³ as defined above in claim 2 in the legend
of formula (I), R³ also possibly representing
hydrogen or a cation capable of forming a salt with
COO⁻, this cation preferably being Na⁺, K⁺ or Li⁺.

- 15 6. A crosslinked collagenic peptide, characterized
• in that it comprises collagenic chains linked
20 together by disulfide bridges in which the
constituent sulfur atoms belong to mercaptoamino
residues that are exclusively grafted onto the
aspartic acids and glutamic acids of the
collagenic chains via amide bonds
• in that it is obtained from the collagenic peptide
25 as claimed in claim 4 and/or 5.

- 30 7. The collagenic peptide according to any one of
claims 1 to 6, characterized in that it comprises
grafts G attached to at least some of the free amine
moieties of the collagenic chain, via amide bonds, G
being an acyl comprising a hydrocarbon-based
species, WITH THE EXCLUSION of the mercaptoamino
residues, in particular those as defined above, this

hydrocarbon-based species, optionally comprising hetero atoms (advantageously O and/or N) and preferably being chosen from alkyls and/or alkenyls and/or alicyclics and/or aromatics and even more preferably from groups comprising an optionally unsaturated alkyl chain, containing from 1 to 22 carbon(s) or corresponding to the formula (III) below:

10 FORMULA (III)



with

- $\text{R}^5 = \text{H}$ or CH_3 ;
- $\text{R}^6 = \text{H}$ or a linear or branched alkyl and preferably a methyl;
- $z = 0, 1$ or 2 and $n > 0$ and n is chosen such that the molecular weight of the polymer chain is between 100 and 15 000 and preferably between 200 and 8 000.

20

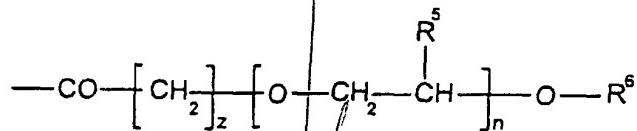
8. A process for obtaining a collagenic peptide which is soluble in aqueous medium and/or in polar solvents and modified by grafting substituted thiol functions borne by mercaptoamino residues, characterized in that it consists essentially in reacting in solution exclusively the carboxylic functions of the aspartic acids and glutamic acids of a collagenic peptide with at least one precursor of a mercaptoamino residue in which the thiol function and the possible carboxylic function are blocked, in the presence of at least one grafting agent preferably chosen from the group comprising

AMENDED SHEET

Newly filed

species optionally comprising hetero atoms (advantageously O and/or N) and preferably being chosen from alkyls and/or alkenyls and/or alicyclics and/or aromatics and even more preferably from groups comprising an optionally unsaturated alkyl chain, containing from 1 to 22 carbon(s) or corresponding to the formula (III) below:

5 FORMULA (III)



- R⁵ = H or CH₃;
- R⁶ = H or a linear or branched alkyl radical and preferably a methyl;
- z = 0, 1 or 2 and n > 0.

10 8. A process for obtaining a collagenic peptide which
15 is soluble in aqueous medium and/or in polar
20 solvents and modified by grafting substituted thiol
functions borne by mercaptoamino residues,

25 characterized in that it consists essentially in reacting in solution the collagenic peptide with at least one precursor of a mercaptoamino residue in which the thiol function and the possible carboxylic function are blocked, in the presence of at least one grafting agent preferably chosen from the group comprising products that activate carboxylic groups, preferably carbodiimides.

30 9. A process for preparing a crosslinkable collagenic peptide, modified by grafting free thiol functions

products that activate carboxylic groups, preferably carbodiimides.

9. A process for preparing a crosslinkable collagenic peptide, modified by grafting free thiol functions borne by mercaptoamino residues, characterized in that it consists essentially:
1. in reacting in solution exclusively the carboxylic functions of the aspartic acids and glutamic acids of a collagenic peptide with at least one precursor of a mercaptoamino residue whose thiol function and possible carboxylic function are blocked, in the presence of at least one grafting agent preferably chosen from the group comprising products that activate carboxylic groups, preferably carbodiimides,
2. and in deprotecting (conversion to thiols) the mercapto functions of the mercaptoamino residues grafted onto the modified collagenic peptides obtained in step 1.
10. A process for preparing a crosslinked collagenic peptide from a collagenic peptide modified by grafting free thiol functions borne by mercaptoamino residues, characterized in that it consists essentially:
1. in reacting in solution exclusively the carboxylic functions of the aspartic acids and glutamic acids of a collagenic peptide with at least one precursor of a mercaptoamino residue whose thiol function

and possible carboxylic function are blocked, in the presence of at least one grafting agent preferably chosen from the group comprising products that activate carboxylic groups, preferably carbodiimides,

- 5
- 10
- 15
- 20
- 25
- 30
11. The process according to any one of claims 8 to 10, characterized in that an additional step F is envisaged, this being a step of functionalization with grafts G that are different in nature from the grafts attached to the carboxylic functions of the aspartic acids and glutamic acids, this step F consisting essentially in carrying out an acylation of at least some of the free amine functions of the collagenic chain, so as to attach thereto grafts G comprising a hydrocarbon-based species, so as to attach to these amines grafts G comprising a hydrocarbon-based species, this species optionally comprising hetero atoms (advantageously O and/or N) and preferably being chosen from alkyls and/or alkenyls and/or alicyclics and/or aromatics.
12. Use of the collagenic peptides according to any one of claims 1 to 7 or of the peptide obtained by the

process according to any one of claims 8 to 11, as a biomaterial which is a constituent of implants, prostheses, dressings, artificial tissues, a bioencapsulation system, a biocompatibilizing coating, suture threads, adhesives or surgical cements or a cell culture support.

5
RPA
AI